

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A prospective cohort study to investigate parental stress and child health in low-income Chinese families: protocol paper
AUTHORS	Wong, Rosa Sze Man; Yu, Esther Yee Tak; Guo, Vivian Yawei; Wan, Eric; Chin, Weng Yee; Wong, Carlos; Fung, Colman; Tung, Keith Tsz-Suen; Wong, HSW; Ip, Patrick; Tiwari, Agnes Fung Yee; Lam, Cindy

VERSION 1 – REVIEW

REVIEWER	Alison Parkes' University of Glasgow
REVIEW RETURNED	08-Aug-2017

GENERAL COMMENTS	<p>General comments</p> <p>Two overall aims could be more clearly stated and a research gap evidenced in the Introduction. It could do more to focus on the possible “cycle of ill health between parents and children” (Discussion, page 14) - elaborate more on how children’s mental and physical health may affect parents as well as the more established reverse effect. An additional aims seem to be to explore whether different aspects/measures of parent stress/child health show similar relationships – eg does parenting stress impact child BMI as much as child behaviour problems?</p> <p>Specific comments</p> <p>Page 4</p> <p>Lines 7-8 Explain Gini coefficient. A more up-to-date figure (2016 is available) should be used for this and the proportion living in poverty.</p> <p>Lines 19-36 In this paragraph, there should be a reference to the main theory linking poverty with poor child health outcomes: the Family Stress Model.</p> <p>Lines 48-50 Tautology – suggest remove the last part of the sentence (“ , which influences parents’ well-being and mental health.”)</p> <p>Page 7</p> <p>Paragraph on biological effects of stress on child health. The first 2 sentences of this paragraph are not well integrated into the rest of the text.</p> <p>Line 48 Suggest that the authors give some examples of “biological changes” in children produced by stress, to clarify what is meant here.</p> <p>Line 53 Tautology - suggest remove the second part of this sentence (“ , but these studies focused on stress resulting from parenting”).</p>
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Page 8

Lines 3-19. This paragraph would read more easily if it was separated into two separate and more detailed paragraphs, one on mediators and one on moderators. At present, the two ideas are jumbled together with the bit about mediators sandwiched in between 2 sentences about moderators.

The mediators are not very well argued. Rather than being told about an associations between economic disadvantage and trauma/violence (lines 7-8), we need to know (a) whether parenting stress is associated with child maltreatment, and whether maltreatment in turn predicts child health. Similarly, the argument for maternal quality of life as mediator is not well presented, and there are no citations in support of the idea that family disharmony is a mediator. Would the mediators suggested work equally well for both directions of the parenting stress-child health association?

Pages 9-10

Sample size calculations

I am not a statistician - but could I suggest checking and clarifying the number of factors given (16 including potential confounders)?

The number of measures listed in this study appears to exceed this by some considerable margin, but perhaps 16 is the maximum to be included in any one analysis?

Eligibility criteria/recruitment

Please clarify, in the case of families where both parents and more than one child is eligible, whether there are any further guidelines for selecting a parent-child pair. For example, it might be that overall, a balanced design would be sought with a 50-50 split between fathers and mothers and between boys and girls.

Please also clarify whether intervention and control families for the Family Enhancement Scheme are both eligible for the current study, and if so whether a balanced design will be sought.

Page 10. Line 43 Clarify whether all the questionnaires (I've counted ten different scales in all) are to be administered in a single telephone session, and any piloting of this.

Lines 43-59. Clarify who will complete the 4 scales on the family and neighbourhood environment – the parent, presumably?

Page 11

The Child Health Questionnaire (“primary outcome”) alone has 12 subscales – are all these to be considered as separate primary outcomes? (some subscales, such as family activities and family cohesion might overlap with the mediators).

Page 12. Allostatic load index. Clarify that measures of all the physiological parameters mentioned in lines 28-30 are included in this study.

Page 13

Lines 4-19. Clarify when all covariate measures are collected, and whether any such as household income are time-varying (repeated measures).

Page 13 “Primary outcomes” – since the interest is in bidirectional associations between parental stress and child health, should this not be “primary outcomes/ exposures”?

Page 14

Lines 20-23. Here, measures of smoking and drinking are “among family members”, but on page 13 line 8 it says “parental history of smoking, drinking and illicit drug use”.

Discussion. Limitations should be included here. IN relation to the issue of bias, there could be more comment on the advantages of supplementing questionnaire-based health measures with physical measures and biological markers.

	Throughout this MS, the authors need to correct mistakes in punctuation, past tense, prepositions and use of plural.
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REVIEWER	Dr. Rasheda Khanam Johns Hopkins Bloomberg School of Public Health
REVIEW RETURNED	23-Aug-2017

GENERAL COMMENTS	<p>This study is proposed to investigate parental stress and child health in low-income Chinese families. In general, this is a well written protocol.</p> <p>Specific comments:</p> <ol style="list-style-type: none"> 1. Prospective and cohort are synonymous – please use one or the other in the title. 2. Re introduction section, the problem statement is not adequately quantified. The authors should provide some data in support of their statement. The authors needs to revise the introduction section highlighting the global, regional and then country specific situation around this problem. It is hard to understand the magnitude of the problem without any data on parental stress and child health. 3. Methods and analysis: The authors should add an objective on prevalence of parental stress in the community. 4. How much venous sample and for what purpose were not mentioned. 5. In the methods, authors should clearly explain the consent process and how long it takes to complete the interview. 6. Citation was incomplete: #7 full citation is needed. 7. Analysis plan section should be reviewed by a statistician. <p>Recommendation: Accept after revision.</p>
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REVIEWER	Shi Huang Vanderbilt University Medical Center, Department of Biostatistics USA
REVIEW RETURNED	04-Oct-2017

GENERAL COMMENTS	<p>The relationship between parental stress and child health is an important and timely topic to investigate. Listed below are some suggestions to improve this protocol.</p> <p>Study Aims: I feel the statements of the Aims are vague. For example, what does "to evaluate the stress of parents" mean? Do the authors meant to say that they want to examine if there are significant changes of parents stress over time?</p> <p>Recruitment: It is unclear whether the participants are recruited from both intervention and control group, or only from the control group.</p>
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	<p>If the participants are recruited from the intervention group, the generalizability of the results can be limited.</p> <p>Assessment procedure: Consider adding one more follow-up assessment because the growth curve analysis can be much more flexible with four time-points than that with only three time-points.</p> <p>Collecting sensitive information via a telephone survey can cause response biases. Consider using an audio-CASI system.</p> <p>Study instrument and measures: Psychometric properties, such as Cronbach's alphas need to be reported.</p> <p>Data analysis: 1) ITT is irrelevant because this is an observational study. In addition, ITT is not a way to handle missing data due to attrition. Consider using full information maximum likelihood method. 2) It would be more clear if a figure of the cross-lagged panel model can be presented. 3) In Figure 1, it is unclear what parental stress and child health really represent. Are they the trajectories (i.e., slope) over time? 4) It is unclear how the moderators related to the hypothesized model. Do they only moderate Y on X? Or they can also moderate M on X? Or Y on M? 5) Need to specify the statistical software(s) that will be used.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

General comments

1. Two overall aims could be more clearly stated and a research gap evidenced in the Introduction. It could do more to focus on the possible “cycle of ill health between parents and children” (Discussion, page 14) - elaborate more on how children's mental and physical health may affect parents as well as the more established reverse effect. An additional aims seem to be to explore whether different aspects/measures of parent stress/child health show similar relationships – eg does parenting stress impact child BMI as much as child behaviour problems?

Response: Thank you for your comments. We have elaborated the rationale of the study and stated the research gap in the introduction. We have provided more details on the potential underlying mechanisms from children's health problems to parental stress and also from parental stress to children's problems. While this study does not aim to compare the impact of parental stress on child BMI and that on child behavioral problems, we try to explore different aspects of child health. We hypothesize that economic hardship leads to poor parenting practices, resulting in greater risk of childhood obesity and behavioral problems which are recognized indicators of child health. This rationale of the link between parental stress, poor parenting practices and child health problems has been added to the Introduction (P.4-5, cleaned version of revised manuscript).

Specific comments

Page 4

2. Lines 7-8 Explain Gini coefficient. A more up-to-date figure (2016 is available) should be used for this and the proportion living in poverty.

Response: Gini coefficient is the most commonly used measure of income inequality in a place or country. Higher Gini coefficient is related to worse average population health (1). In 2016, Hong Kong has a high Gini coefficient of 0.539. The relevant statement has been revised to include this updated figure in the Introduction (P.4. cleaned version of revised manuscript).

Reference:

1. Subramanian SV, Kawachi I. Income inequality and health: what have we learned so far? *Epidemiologic reviews* 2004;26(1):78-91.

3. Lines 19-36 In this paragraph, there should be a reference to the main theory linking poverty with poor child health outcomes: the Family Stress Model.

Response: Thanks to the reviewer for suggesting the Family Stress Model (FSM). We agree that the FSM provides a theoretical framework for our study conceptual model and have added the details of the model to the Introduction (P.4-5, cleaned version of revised manuscript).

4. Lines 48-50 Tautology – suggest remove the last part of the sentence (“, which influences parents’ well-being and mental health.”)

Response: Thank you for pointing this out. We have removed the last part of the sentence.

Page 7

5. Paragraph on biological effects of stress on child health. The first 2 sentences of this paragraph are not well integrated into the rest of the text.

Response: Thank you for the comment. We have revised the paragraph to make it more coherent.

6. Line 48 Suggest that the authors give some examples of “biological changes” in children produced by stress, to clarify what is meant here.

Response: We have added some examples of biological changes in children, including neuroendocrine, epigenetic, and neuroanatomical changes, to clarify the meaning of biological changes was meant there (P.6, cleaned version of revised manuscript).

7. Line 53 Tautology - suggest remove the second part of this sentence (“, but these studies focused on stress resulting from parenting”).

Response: Thank you for pointing this out. We have removed the sentence from the paragraph.

Page 8

8. Lines 3-19. This paragraph would read more easily if it was separated into two separate and more detailed paragraphs, one on mediators and one on moderators. At present, the two ideas are jumbled together with the bit about mediators sandwiched in between 2 sentences about moderators.

Response: Thank you for the comment. We have separated the information into two paragraphs, one for mediation (P.6-7, cleaned version of revised manuscript) and the other for moderation (P.7, cleaned version of revised manuscript).

9. The mediators are not very well argued. Rather than being told about an associations between economic disadvantage and trauma/violence (lines 7-8), we need to know (a) whether parenting stress is associated with child maltreatment, and whether maltreatment in turn predicts child health. Similarly, the argument for maternal quality of life as mediator is not well presented, and there are no citations in support of the idea that family disharmony is a mediator. Would the mediators suggested work equally well for both directions of the parenting stress-child health association?

Response: Thank you for pointing this out. We have added the references on the association between parental stress and child maltreatment (P.6, cleaned version of revised manuscript) and between maltreatment and child health (P. 4-5 & P.6-7, cleaned version of revised manuscript). Maternal quality of life is considered as outcome rather than mediator in this study. For potential mediators such as family disharmony, more citations have been added to support the argument in the Introduction (the rationale can be found in P.6-7, cleaned version of revised manuscript). We hypothesize that parental stress leads to child health problems through family disharmony, as we would like to focus this study on child health and parental stress, and hence the potential mediators should be intermediate variables linking parental stress and child health to each other. We would also explore mechanisms that work in the other direction.

Pages 9-10

Sample size calculations

10. I am not a statistician - but could I suggest checking and clarifying the number of factors given (16 including potential confounders)? The number of measures listed in this study appears to exceed this by some considerable margin, but perhaps 16 is the maximum to be included in any one analysis?

Response: Yes, the reviewer is correct that there will only be at most 16 factors included in a single path model. The study will collect on as many plausible factors as feasible and we shall select the most relevant ones in the analysis of any single model to take into account of the conceptual (e.g. only one outcome for each model) and technical (e.g. multicollinearity) constraints.

Eligibility criteria/recruitment

11. Please clarify, in the case of families where both parents and more than one child is eligible, whether there are any further guidelines for selecting a parent-child pair. For example, it might be that overall, a balanced design would be sought with a 50-50 split between fathers and mothers and between boys and girls.

Response: We recruited one parent-one child pairs for our study with identification of an index child aged 6 to 18 years who had undergone a cognitive assessment on recruitment. The primary custodial parent (i.e. the parent spending a majority of the time with the index child) was selected as the study subject regardless of their gender. More details on the guidelines for selecting a parent-child pair have been added to the Eligibility Criteria section (P.9, cleaned version of revised manuscript). As we have a relatively small number of eligible families, it will not be possible to conduct a balanced design.

12. Please also clarify whether intervention and control families for the Family Enhancement Scheme are both eligible for the current study, and if so whether a balanced design will be sought.

Response: Yes, we include all families in both intervention and control groups in this study. The small number of families does not allow a balanced design, but we shall adjust for the grouping effect in the data analyses. We have added the information to the Maintenance Strategies section (P.11, cleaned version of revised manuscript)

13. Page 10. Line 43 Clarify whether all the questionnaires (I've counted ten different scales in all) are to be administered in a single telephone session, and any piloting of this.

Response: The questionnaires had been pilot-tested in several low-income parents prior to the main study and minor editing was done to ensure the questionnaires are comprehensible to the respondent. The questionnaires will be administered in two separate batches – the first includes the SF-12, DASS, CHQ and SDQ; the second includes the family/neighborhood questionnaires. They will be administered by trained interviewers by face-to-face interview or telephone multiple sessions. Such information has been added to the Recruitment section (P.9-10, cleaned version of revised manuscript).

14. Lines 43-59. Clarify who will complete the 4 scales on the family and neighbourhood environment – the parent, presumably?

Response: Yes, the parent will complete the 4 scales on the family and neighbourhood environment and this information has been provided in the Recruitment section (P.10, cleaned version of revised manuscript).

Page 11

15. The Child Health Questionnaire (“primary outcome”) alone has 12 subscales – are all these to be considered as separate primary outcomes? (some subscales, such as family activities and family cohesion might overlap with the mediators).

Response: This study will use Child Health Questionnaire General Health Perception subscale scores as the primary exposure/outcome (P.14, cleaned version of revised manuscript). We shall evaluate other subscale scores as secondary outcomes.

16. Page 12. Allostatic load index. Clarify that measures of all the physiological parameters mentioned in lines 28-30 are included in this study.

Response: Yes, all of the physiological parameters mentioned, i.e. blood pressure, heart rate, BMI, waist-to-hip ratio, lipid profile, fasting glucose and glycosylated haemoglobin will be included in the calculation of the allostatic load index.

Page 13

17. Lines 4-19. Clarify when all covariate measures are collected, and whether any such as household income are time-varying (repeated measures).

Response: Parental history of smoking, drinking and illicit drug use, occupation and marital status, comorbidities of parents and children, and household income will be measured at baseline and follow-ups. Children's cognitive skills were measured at baseline only, as cognitive skills are relatively static across time. Other sociodemographic characteristics (children's age and gender, and parental age and gender, education level, and immigration status) will be measured only at baseline. This information has been added to the Study Instrument and Measures section (P.13, cleaned version of revised manuscript).

18. Page 13 “Primary outcomes” – since the interest is in bidirectional associations between parental stress and child health, should this not be “primary outcomes/ exposures”?

Response: Thank you for pointing this out. We have revised “primary outcomes” to “primary outcomes/exposures” (P.14, cleaned version of revised manuscript).

Page 14

19. Lines 20-23. Here, measures of smoking and drinking are “among family members”, but on page 13 line 8 it says “parental history of smoking, drinking and illicit drug use”.

Response: Thanks to the reviewer for pointing out this discrepancy. We have revised and consistently used “parental history of smoking, drinking and illicit drug use” throughout the main text.

20. Discussion. Limitations should be included here. IN relation to the issue of bias, there could be more comment on the advantages of supplementing questionnaire-based health measures with physical measures and biological markers.

Response: Thank you for the comments. We have added a paragraph on strengths and limitations of the study in Discussion section (P.16, cleaned version of revised manuscript).

21. Throughout this MS, the authors need to correct mistakes in punctuation, past tense, prepositions and use of plural.

Response: Thank you for pointing this out. We shall proofread the text again carefully.

Reviewer: 2

This study is proposed to investigate parental stress and child health in low-income Chinese families. In general, this is a well written protocol.

Response: Many thanks to the reviewer for the positive comments.

Specific comments:

1. Prospective and cohort are synonymous – please use one or the other in the title.

Response: Thank you for the comment and we agree that cohort studies are usually prospective but there are studies that analyze retrospective data of cohorts. We would like to keep the term “prospective cohort” in the title so as to differentiate it from retrospective design.

2. Re introduction section, the problem statement is not adequately quantified. The authors should provide some data in support of their statement. The authors need to revise the introduction section highlighting the global, regional and then country specific situation around this problem. It is hard to understand the magnitude of the problem without any data on parental stress and child health.

Response: Thank you for the suggestion. We have elaborated on the rationale with more specific information on the high prevalence of parental stress and poor child HRQOL in low income families. We have also explained the research gap about the association between parental stress and child health risks in first paragraph of the introduction session (P.4, cleaned version of revised manuscript).

3. Methods and analysis: The authors should add an objective on prevalence of parental stress in the community.

Response: Thank you for the suggestion. We will use DASS Stress subscale to measure parental stress, and estimate the prevalence of mild to high stress in low-income parents based on the recommended cut-off scores in the DASS manual. The objective has been added under Study Aims section (P.8, cleaned version of revised manuscript).

4. How much venous sample and for what purpose were not mentioned.

Response: We will collect 15ml of venous sample from each adult subject in the study at baseline, 12 months and 24 months to measure blood lipid profile, fasting glucose and glycosylated haemoglobin for the calculation of their allostatic load.

5. In the methods, authors should clearly explain the consent process and how long it takes to complete the interview.

Response: Thank you for pointing this out. We have added a detailed explanation on the consent process and interview process and duration in the Recruitment section (P.10, cleaned version of revised manuscript).

6. Citation was incomplete: #7 full citation is needed.

Response: Thanks to the reviewer for pointing out this mistake. The citation has been updated.

7. Analysis plan section should be reviewed by a statistician.

Response: Thank you for the comment. The analysis plan has been reviewed and revised by a statistician again carefully.

Reviewer: 3

The relationship between parental stress and child health is an important and timely topic to investigate. Listed below are some suggestions to improve this protocol.

Study Aims:

1. I feel the statements of the Aims are vague. For example, what does "to evaluate the stress of parents" mean? Do the authors meant to say that they want to examine if there are significant changes of parents stress over time?

Response: Thanks to the reviewer for pointing this out. We have stated the aims more specifically and clearly.

Recruitment:

2. It is unclear whether the participants are recruited from both intervention and control group, or only from the control group. If the participants are recruited from the intervention group, the generalizability of the results can be limited.

Response: We will recruit on all eligible parent-child pairs from both intervention or control families of the Family Enhancement Scheme project. The potential grouping effect will be adjusted in the data analyses. The information has been added to the Maintenance Strategies section (P.11, cleaned version of revised manuscript)

Assessment procedure:

3. Consider adding one more follow-up assessment because the growth curve analysis can be much more flexible with four time-points than that with only three time-points.

Response: We agree that more follow-up assessment will give a more flexible growth curve analysis, but we have to balance this against respondent burden (and response rate) in the completion of the large number of questionnaires. Therefore, we have decided to measure the outcomes at 3 time points, which is the minimum for a cross-lagged panel analysis model, in this study. Nonetheless, we have stated in the Discussion section that further follow-up assessment should be conducted if resources are available (P.16, cleaned version of revised manuscript).

4. Collecting sensitive information via a telephone survey can cause response biases. Consider using an audio-CASI system.

Response: Thanks to the reviewer for the suggestion. Our experience found that many people did not accept interviews by audio-CASI system because it is impersonal and our participants may not have the digital literacy skills to use the system. We have not included questions on sensitive information such as substance abuse or domestic violence in the telephone interview. These sensitive data will be collected by face-to-face interview when the subjects attend the physical examination or blood taking.

Study instrument and measures:

5. Psychometric properties, such as Cronbach's alphas need to be reported.

Response: Thanks to the reviewer for the suggestion. The information has been added to the section on Study Instrument and Measures (P. 11-13, cleaned version of revised manuscript).

Data analysis:

1) ITT is irrelevant because this is an observational study. In addition, ITT is not a way to handle missing data due to attrition. Consider using full information maximum likelihood method.

Response: Thank you very much for pointing out our inappropriate use of the term "ITT". As suggested, we have revised the relevant data analysis section to the "use of full information maximum likelihood" to handle missing data (P.13, cleaned version of revised manuscript).

2) It would be more clear if a figure of the cross-lagged panel model can be presented.

Response: Thank you for the suggestion. The cross-lagged panel model has been added as Figure 2.

3) In Figure 1, it is unclear what parental stress and child health really represent. Are they the trajectories (i.e., slope) over time?

Response: Yes they are the trajectories over time. The child health (i.e. the CHQ General Health Perception subscale score) and parental stress (i.e. DASS Stress subscale score) will be measured repeatedly in all three time points. The primary hypothesis using latent growth modelling will model how variables change over time. The model specification will use the raw unmanipulated form (but not the change) as the dependent variable. This has been clarified in the Data Analysis section (P.13, cleaned version of revised manuscript).

4) It is unclear how the moderators related to the hypothesized model. Do they only moderate Y on X? Or they can also moderate M on X? Or Y on M?

Response: Our hypothesis is that the moderators moderate Y on X (the primary association). We will also explore whether they can also moderate M on X or Y on M. This has been clarified in the Data Analysis section (P.14, cleaned version of revised manuscript).

5) Need to specify the statistical software(s) that will be used.

Response: Thank you for pointing out this missing information. IBM SPSS Statistics and Mplus will be used for data analysis, which has been specified in the Data Analysis section (P.14, cleaned version of revised manuscript).

VERSION 2 – REVIEW

REVIEWER	Shi Huang Vanderbilt University Medical Center
REVIEW RETURNED	30-Nov-2017
GENERAL COMMENTS	Thanks for revising the manuscript accordingly. My only comment is to take out the following sentence from the protocol because it is the same as the growth curve analysis. "Linear mixed effect model, including subjects as random effects, will be performed to evaluate the association between parental variables and between children's variables."

VERSION 2 – AUTHOR RESPONSE

Thanks for revising the manuscript accordingly. My only comment is to take out the following sentence from the protocol because it is the same as the growth curve analysis.
"Linear mixed effect model, including subjects as random effects, will be performed to evaluate the association between parental variables and between children's variables."

Response: Thank you for your comment. We have deleted the sentence from the protocol accordingly.